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Dr. Joshua Lederberg
The Rockefeller University
1230 York Avenue
New York, NY 10021

Dear Josh:

Quite belatedly, I'm sending you several reprints on the switching phenomenon in Candida. We have a paper we're about to submit on the genetics of the process; I'll send you that one as soon as it's ready to go to the journal.

As you can see, there are two kinds of switching: one affects the regulation of the yeast-to-hyphal transition (the colony morphology switch), while the other (the white-opaque transition) causes cells to switch back and forth between a normal and an abnormal cell shape. Their common characteristics are that they can occur with roughly the same frequency (10^{-4}-10^{-5} per cell division) and that both are recessive. They differ in several ways: induction of colony morphology switching (CM) variants appears to be possible even from strains that don't make hyphae very well; the hyphal products appear to be normal, and there is a variety of different phenotypes, depending (probably) on exactly how the yeast to hyphal transition is affected. Furthermore, these phenotypes are accessible from each other - the cells don't have to go back to the 100% yeast form in order to go from "star" to "hat."

The white-opaque transition is only found in a few strains and so far as I know no one has succeeded in inducing it with mutagenesis. Opaque cells contain antigens that are all their own, and there are only two phenotypes. Opaque cells have a peculiar surface, which is not well understood.

We have mapped some "switching" genes for WO (the white-opaque switch) to the third chromosome; using spheroplast fusion and parasexual genetics we can show that loss of the homologues of this chromosome which come from the switching parent causes cells to lose the ability to switch. Furthermore, UV-induced mitotic crossing-over, leading to homozygosis along some part of chromosome 3 also gave some non-switchers. Attempts to transform the non-switching crossover products with a library from the switching parent worked too well. Transformation with a variety of plasmids (including rDNA!) gave switching transformants, although not with a frequency much better than 10% for any given plasmid. So somehow transformation induces switching in a stochastic way, and it does it by a mechanism that doesn't include whatever is on chromosome 3 in the switching strain. If this makes sense to you, let me know. It doesn't to me. I'm at the stage of tolerating ambiguity while we try to map the switching locus (if that's what it is) more precisely on chr. 3.

I hope you find all this vaguely interesting. It was fun to talk to you and to hear about your new stuff at the Adelberg Symposium.

Yours,
Pete

P. T. Magee
Dean

PTM:lcc
Encl. (6)

- much more than vaguely.
I really appreciate this.
Sincerely,
Josh.